WHAT IS CLAIMED IS:

1. A method of generating a pluripotent mammalian cell, the process comprising the preparation of cytoplast fragments from a mammalian oocyte or fertilized zygote (the cytoplast donor), fusion of a cytoplast fragment with a cell or karyoplast (the nuclear donor) which is taken from any mammalian species.

2. A cell population derived from the method of claim 1.

3. A method according to claim 1, wherein the cytoplast fragments are prepared by a process that includes removing the zona pellucida, treatment of the cytoplast donor with a microfilament inhibitor, and fragmentation into cytoplasts by vortexing, or micropipetting, or manual slicing with a suitable micromanipulation tool.

4. A method according to claim 1 further comprising enucleating the cytoplast donor prior to fragmentation.

5. A method according to claim 1, wherein the cytoplast donor is an activated, low MPF (interphase) oocyte, or an aged, unactivated, low MPF, oocyte, or most preferred, an unactivated, high MPF, metaphase II oocyte.

6. A method according to claim 1, wherein the cytoplast donor is from a different species from that of the nuclear donor.

7. A method according to claim 1, wherein the cytoplast donor is from the same species as that of the nuclear donor.

Sub a1 8. A method as claimed in any of claims 1-7, wherein the cytoplast donor is derived from any non-human mammalian species, but preferably from mouse, rat, rabbit, sheep, goat, pig, or most preferably, cow.

9. A method as claimed in any of claims 1-8, wherein fusion between cytoplast and karyoplast includes one of the following methods: electrical fusion, chemical fusion (i.e., polyethylene glycol or high pH-low osmolarity, virus-mediated fusion (i.e., Sendai virus), liposomes, or fusion mediated by cell surface proteins (i.e., hernaglutinins).

10. A method according to claim 1 further comprising an activation step.

11. A method according to claim 10 wherein the method of activation is selected from one of the following methods: electrical pulse, ionomycin/DMAP, cytochalasin/cyclohexamide, strontium, adenophostin, disintegnin RGD peptide, DDT/thimerosal, or sperm factor.

Sub a2 12. A method according to any of claims 1-11, wherein the cytoplasts are prepared from in vivo or in vitro produced oocytes.

13. A method according to claim 12, wherein the oocytes have been subjected to an in vitro maturation step.

Sub a3 14. A method according to any of claims 1-13, wherein the donor nucleus is from an embryonic, fetal, or adult cell/karyoplast.

15. A method according to claim 14, wherein the donor nucleus is from a diploid cell.

16. A method according to claim 15, wherein the diploid nucleus is provided preferably by a cell/karyoplast synchronized in G0/G1, or by a cell arrested at the G1/S border.

17. A method according to claim 14, wherein the donor nucleus is from a differentiated or undifferentiated stem cell, or somatic cell.

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18. A method according to claims 14-17, wherein the donor nucleus is from a human cell.

19. A method as claimed in any of claims 1-17, wherein the donor nucleus is from a cow or bull, pig, sheep, goat, camel, waterbuffalo, primate, rodent, or lagomorph.

20. A method as claimed in any of claims 1-19, in which the donor nucleus has been genetically modified.

21. A method according to claim 20, wherein the cell used to provide the donor nucleus has been genetically modified, such that the resultant hybrid cell (produced according to claim 1) provides a means to cure or treat animal or human disease.

22. Genetically modified mammalian cells, as referred to in claim 20 (most preferably human cells), which have been stably transfected with genes (i.e., coding for therapeutic proteins such as insulin, clotting factors, erythropoietin, tumor suppressor genes, growth factors, cytokines, therapeutic peptides, or antibodies). Such donor cells would be used to produce hybrid derived populations of cells, which could be differentiated into the cell type most apt for delivery of the therapeutic agent.

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23. A method as claimed in any of claims 1-22, in ~~which the~~ mitochondria of the donor cytoplast is ~~made~~ replication incompetent (i.e., incubation with EtBr or any other inhibitor of mitochondrial DNA replication).

24. A method according to claim 23, wherein the cytoplasts chosen, contain congenital mitochondrial lesions.

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25. A method as claimed in any of claims 1-24, ~~wherein~~ mitochondria derived from the same species ~~(or most preferred, from the same animal or individual)~~ as the nuclear donor, are used to supplement the mitochondria present in the hybrid cell.

26. A method according to claim 25, wherein the mitochondria are supplemented via fusion of an enucleated cytoplast (which is derived from the same species/animal/individual as the nuclear donor) with a previously formed (according to claim 1) hybrid cell or couplet.

27. A method according to claim 26, wherein the anucleate cytoplast, used for fusion to the hybrid cell, is derived from mitochondria-rich, blood-derived platelets (again the platelets would be derived from the same species/animal/individual, as the nuclear donor).

28. A method according to claim 20, wherein genes encoding mitochondrial maintenance factors (i.e., mtTFA), are stably transfected into the cells used as nuclear donors, as a means to facilitate survival of trans-species mitochondria.

29. A method according to claim 20, wherein genes encoding modulators of histone acetylation and chromatin structure, are transiently expressed in nuclear donor cells, as a means to compromise the transcriptional

apparatus of the donor cells, thus creating an environment conducive to chromatin reprogramming in resulting hybrids.

30. A method according to claim 27, wherein the gene used for general downregulation of gene transcription in the donor cell/karyoplast is histone deacetylase, which in the preferred method, is transfected into the donor cell prior to hybrid production, in order to facilitate reprogramming upon contact with the components contained in the cytoplast fragment.

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31. A method as claimed in any of claims 1-30, wherein ~~already-~~ established populations of hybrid-derived cells ~~(HDCs)~~, are cultured in the presence of compounds or factors known to induce gene transcription, as a means to assist the HDC genome in activation of gene transcription.

32. A method according to claim 31, wherein the inducers of gene transcription are reversible inhibitors of histone deacetylase, including butyrate, or in a more preferred method, trichostatin A.

33. A method according to claim 31, wherein HDCs are cultured in a medium that is appropriate to support development and proliferation, while maintaining a dedifferentiated state.

34. A method according to claim 33, wherein HDCs are cultured in a medium containing growth factors and cytokines, including LIF, stem cell factor, and/or GCT44 (human yolk sac teratoma cell factor).

35. A method according to claim 33, wherein HDCs are cultured in the presence of mitotically-inactivated primary cell feeder cell layers, as a means to facilitate growth, while maintaining an undifferentiated state.

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36. A method as claimed in any of claims 1-35, wherein already established populations of HDCs are removed from culture conditions intended to prevent differentiation (according to claims 33-35), and are induced to differentiate, by culture in the presence of chemicals and factors known to induce differentiation of cells to become specific lineages.

37. A method according to claim 36, wherein HDCs are cultured in the presence of factors known to induce neural pathway differentiation, including retinoic acid, fibroblast growth factor 2 (FGF2), epidermal growth factor (EGF), and plateletderived growth factor (PDGF).

38. A method according to claim 36, wherein HDCs are cultured in the presence of c-kit and erythropoietin, to induce the development of erythrocyte precursors.

39. A method according to claim 36, wherein HDCs are cultured in the presence of macrophage colony stimulating factor (M-CSF) and interleukin 1, and interleukin 3, to induce development of macrophage precursors.

40. A method according to claim 36, wherein HDCs are cultured in the presence of retinoic acid, insulin, and tri-odothyronine, to induce development of adipocytes.

41. A method according to claim 36, wherein HDCs are cultured in the presence of retinoic acid plus dibutyrl cyclic AMP, to induce development of heart vascular smooth muscle cells.

42. A method according to claim 36, wherein HDCs are co-cultured in the presence of cells from the pancreatic bud, in order to induce differentiation to become pancreatic cell precursors, for insulin production.

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43. A method according to claim 35, wherein HDCs, or cells subsequently derived from HDCs (according to claims 36-42), are transfected with genes encoding specific gene activators or transcription factors (i.e., Myo D, or PPAR gamma, or C/EBP alpha), as an alternative means of inducing lineage-specific differentiation.

44. A method according to claims 1-43, wherein the HDCs are used as nuclear donors to clone an organism by nuclear transfer.

45. A method according to claims 1-43, wherein the HDCs are used as donor cells to produce chimeric organisms.

46. A method of preparing and enriching a population of pluripotent cells comprising:

staining with a stain having a first color the cytoplasm of a population of oocytes or fertilized zygotes prior to fragmentation of said oocytes or fertilized zygotes into a population of cytoplasts to;

fragmenting said population of oocytes or fertilized zygotes to produce a population of stained cytoplasts;

transfecting a population of donor cells with a gene that encodes a fluorescent protein fluorescing a second color to produce a population of donor cells transfected with a gene encoding a fluorescent protein;

fusing said population of stained cytoplasts and said population of nuclear donor cells transfected with a gene encoding a fluorescent protein in order to produce a population of cells comprising fusion products, unfused

cytoplasts, unfused nuclear donors, wherein said fusion products comprise hybrid cells with a normal karyotype and aneuploidy cells;

sorting the population of cells by selecting for fusion products and unfused cytoplasts by selecting for cells marked by the first color; and

further sorting the fusion products by selecting for cells with a normal karyotype and marked by the second color.

47. A method of preparing and enriching a population of pluripotent cells comprising:

staining with a stain having a first color the cytoplasm of a population of oocytes or fertilized zygotes prior to fragmentation of said oocytes or fertilized zygotes into a population of cytoplasts to;

fragmenting said population of oocytes or fertilized zygotes to produce a population of stained cytoplasts;

staining the DNA of a population of donor cells with a DNA stain having a second color to produce a population of stained donor cells having DNA stained with the second color;

fusing said population of stained cytoplasts and said population of stained donor cells in order to produce a population of cells comprising fusion products, unfused cytoplasts, unfused nuclear donors, wherein said fusion products comprise hybrid cells with a normal karyotype and aneuploidy cells;

sorting the population of cells by selecting for fusion products and unfused cytoplasts marked by the first color; and

further sorting the fusion products by selecting for cells with a normal karyotype marked by the second color.

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